REMARKS

Claims 1-9 and 17 were pending in the subject application. By this Amendment, applicants have canceled claims 2-7 without prejudice, and added new claims 18 and 19. Accordingly, claims 1, 8, 9 and 17-19 are currently pending and under examination.

Rejection under 35 U.S.C. § 112, second paragraph

On pages 2-3 of the January 10, 2007 Final Office Action, the Examiner maintained the rejection of claims 1-9 under 35 U.S.C. § 112, second paragraph, but indicated that this rejection would be withdrawn if applicants amended the claims to recite that sFRP-5 has the sequence set forth in SEQ ID NO. 1.

In response, applicants have amended the claims to recite that sFRP-5 has the sequence set forth in SEQ ID NO. 1. Accordingly, the rejection under 35 U.S.C. § 112, second paragraph, is moot.

Rejection under 35 U.S.C. § 112, first paragraph

-Written Description

On pages 3-4 of the January 10, 2007 Final Office Action, the Examiner rejected claims 1-9 and 17 as failing to comply with the written description requirement. The Examiner did acknowledge that "the sFRP-5 peptide of SEQ ID NO:1 meets the written description guidelines."

In response, applicants have amended the claims to recite that sFRP-5 has the sequence set forth in SEQ ID NO. 1. Accordingly, the rejection under 35 U.S.C. § 112, first paragraph, is moot.

Rejection under 35 U.S.C. § 112, first paragraph

-Enablement

On page 4 of the January 10, 2007 Final Office Action, the

Examiner rejected claims 1-6, 8-9 and 17 under 35 U.S.C. § 112, first paragraph, on the basis that the specification allegedly does not reasonably provide enablement for reducing the amount of adipose tissue in a subject by administering to the subject an effective amount of an sFRP-5 peptide of SEQ ID NO:1 or a peptide that has (I) 90% identity to the sequence of SEQ ID NO:1, (ii) 91% identity to the sequence of SEQ ID NO:1, (iii) 92% identity to the sequences of SEQ ID NO:1, (iv) 95% identity to the sequence of SEQ ID NO:1, and (v) 99% identity to the sequence of SEQ ID NO:1. The Examiner did acknowledge that the subject application is enabling for administering the sFRP-5 peptide having SEQ ID NO. 1 to reduce adipose tissue.

In response, applicants have amended the claims to recite that sFRP-5 has the sequence set forth in SEQ ID NO. 1. Accordingly, the rejection under 35 U.S.C. § 112, first paragraph, is moot.

Rejection under 35 U.S.C. § 102(e)

On page 5 of the January 10, 2007 Final Office Action, the Examiner maintained the rejection of claims 1-9 and 17 as allegedly anticipated by Xu et al. (US 2003/0143610). The Examiner alleged that Xu et al. teach using SARP3, which the Examiner considered to be identical to sFRP-5, for modulating SARP3 mediated diseases, referring to the abstract. The Examiner also alleged that Xu et al. teach "administering to a subject having a metabolic disorder comprising SARP-3 polypeptide of SEQ ID NO:2 [0018]."

In response, applicants respectfully traverse this rejection on the basis that Xu et al. fail to teach applicants' claimed invention. Xu et al. at best provide a research plan for investigating the utility and properties of the SARP3 polypeptide, which utility and properties Xu et al. do not teach

and certainly do not enable.

Initially, in response to the Examiner's assertion in the concluding sentence of the rejection on page 5 that "it can be assumed that the product will inherently perform the claimed process", applicants respectfully submit that inherent anticipation cannot be a basis for this rejection. As the Examiner is aware, a rejection based on inherent anticipation requires a showing that "the missing descriptive matter is necessarily present in the thing described in the reference." See, e.g. M.P.E.P. § 2112. However, Xu et al. does not describe a method in which sFRP-5 is actually administered to a subject. The Examiner does not contest this fact about Xu et al. Therefore, in Xu et al. the sFRP-5 did not inherently do anything at all. Thus, because sFRP-5 was not actually administered to a subject in Xu et al., the claimed method was never practiced in Xu et al., no effect of any type occurred in Xu et al., and the necessity requirement of an inherent anticipation is not satisfied.

Furthermore, Xu et al. cannot anticipate, inherently or otherwise, the administration of an amount of sFRP-5 peptide "effective" to reduce the level of adipose tissue. This element of applicants' claimed invention is plainly absent from Xu et al.

Turning now to the 2 sections of Xu et al. referenced by the Examiner, namely: 1) the abstract, and 2) paragraph [0018] of the published patent application. The abstract of Xu et al. fails to teach how to use the SARP3 polypetide. In the only sentence in the abstract where Xu et al. mention SARP3, Xu et al. omit to provide an affirmative step in the method Xu et al. purport to provide (Xu et al., abstract, fifth sentence: "In addition, the invention provides a method for treating a subject having a

metabolic disorder characterized by aberrant SARP3 polypeptide activity or aberrant SARP3 nucleic acid expression.") This sentence fails to describe any step, and as such fails to teach a method. Accordingly, the abstract of Xu et al. fails to teach every element of applicants' claimed invention.

Turning to paragraph [0018] of Xu et al., it becomes apparent that Xu et al. teach nothing about the utility of the SARP3 peptide. Applicants reproduce paragraph [0018] of Xu et al. below:

> [0018] In yet another aspect, the invention features a method for treating a subject having a metabolic disorder characterized by aberrant SARP3 polypeptide activity or aberrant SARP3 nucleic acid expression, e.g., obesity, diabetes, anorexia, or cachexia. The method includes administering to the subject a SARP3 modulator, e.g., in a pharmaceutically acceptable formulation or by using a gene therapy vector. Embodiments of this aspect of the invention include the SARP3 modulator being a small molecule, an anti-SARP3 antibody, a SARP3 polypeptide comprising the amino acid sequence of SEQ ID NO:2 or 5 or a fragment thereof, a SARP3 polypeptide comprising an amino acid sequence which is at least 90 percent identical to the amino acid sequence of SEQ ID NO:2 or 5, an isolated naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of SEQ ID NO:2 or 5, an antisense SARP3 nucleic acid molecule, a nucleic acid molecule of SEQ ID NO: 1, 3, 4, or 6 or a fragment thereof, or a ribozyme.

Paragraph [0018] of Xu et al. mentions the SAPR3 peptide among a laundry list of purported SARP3 modulators. To the extent paragraph [0018] of Xu et al. provides a generic disclosure, there is no basis on record for the selection of applicants' specific peptide recited in the claims.

More importantly, Xu et al. fail to assign an activity to any

member of the laundry list of purported SARP3 modulators. One of skill in the art, therefore, would have no basis for using any member in the laundry list.

Most importantly, paragraph [0018] Xu et al. fails to teach how a purported modulator would "modulate" SARP3. This deficiency in Xu et al. makes it impossible for one of skill in the art to tell from paragraph [0018], or elsewhere in Xu et al., whether to increase or decrease the SARP3 peptide in the subject.

No further teaching about the SARP3 peptide is provided in Xu et al. One skilled in the art could not practice a method for reducing adipose tissue in a subject based on the disclosure of Xu et al.

Accordingly, Xu et al. does not enable applicants' claimed invention.

Furthermore, Xu et al. were not in possession of the invention which applicants claim.

Examiner Gyan Chandra has come to similar conclusions about the aforementioned deficiencies of Xu et al., and the Examiner has eloquently discussed the deficiencies in a May 16, 2006 Office Action in Xu et al.(U.S. Serial No. 10/338,604).[1] A copy of the May 16, 2006 Office Action from the file history of Xu et al. is attached as **Exhibit A** hereto.

In summary, applicants respectfully submit that a non-enabling

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[1] U.S. Serial No. 10/338,604, Xu et al., is indicated as being abandoned on the PAIR records of the U.S. Patent Office for failure of Xu et al. to reply to Examiner Chandra's May 16, 2006 Office Action.

disclosure cannot anticipate; and Xu et al. is a non-enabling disclosure with respect to the subject matter claimed by applicants. Furthermore, applicants respectfully submit that a reference cannot anticipate that which the reference itself is not in possession of; and Xu et al. were not in possession of applicants' claimed invention. Applicants also submit that a generic disclosure cannot anticipate a species unless selection of that species is suggested; and Xu et al. fail to suggest the selection of the specific peptide recited in applicants' claims. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. § 102 based on Xu et al.

No fee is deemed necessary in connection with the filing of this Amendment. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:
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Gary J. Gershik 1/26/07
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EXAMINER	
CHANDRA, GYAN	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 05/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)	
10/338,604	XU, HAIYAN	
Examiner	**Art Unit**	
Gyan Chandra	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *1-8 and 12-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/15/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II, claims 9-11 and species "the ability to modulate lipid metabolism" in the reply filed on 03/01/2006 is acknowledged. However, Applicant did not distinctly and specifically points out the supposed error in the restriction requirement.

The requirement is still deemed proper and is therefore made FINAL.

Status of Application, Amendments, And/Or Claims

Claims 1-20 are pending. Claims 1-8, and 12-20 are withdrawn from further consideration as being drawn to a nonelected Invention.

Claims 9-11 are examined on the merit to the extent that they read on the elected species the ability to modulate lipid metabolism.

Information Disclosure Statement

The information disclosure statement (IDS) filed on 4/15/2005 has been considered.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, see page 59, lines 8 and 11. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

Claim 9 is objected for the use of many abbreviated phrases (SARP3), which should be described for the first time followed by an abbreviated form placed in a bracket. Appropriate correction is required.

Claim Rejections - 35 USC § 101 and 35 USC § 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-11 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility. Novel biological molecules lack a well established utility and must undergo extensive experimentation.

Specifically, claims 9-11 are directed to a method of modulating a SARP3 mediated activity comprising contacting a cell or a tissue that expresses SARP3 with a SARP3 modulator that can modulate lipid metabolism. However, the instant specification does not teach any significance or functional characteristics of the polypeptide SARP3. The specification also does not disclose any specific methods or

working examples for modulating lipid metabolism. The specification discloses in general how a skilled artisan can different screening methods to identify a compound for any known protein that has a known biological function, but fails to show if the instantly claimed polypeptide has any such an impact. Since the utility is not presented in mature form and significant further research is required, the utility is not substantial. The specification asserts the following as patentable utilities for the claimed polypeptide SARP3:

1) to prepare an antibody (pg 63-66);

2) to screen modulators of SARP3 activity (pg 8-20);

3) to detect metabolic disorders (page 20-28); and

4) to treat subjects suffering from metabolic disorders (pg 34-41)

Each of these shall be addressed in turn.

1) to prepare an antibody. This asserted utility is not specific or substantial. An antibody can be prepared for any protein and it is a routine in the art. Further, the specification discloses nothing specific or substantial for the SARP3 polypeptide where this antibody can be used. The use of an antibody for binding the protein against which it is raised is of the type of experimentation that does not meet the requirements of 35 USC § 101.

2) to screen modulators of SARP3. This asserted utility is not specific or substantial. The specification discloses methods to screen for a compound that can modulate a polypeptide SARP3 activity. Since the polypeptide itself does not have any

known activity, the methods of screening using the SARP3 are not presented in a ready to use, real-world application, and the asserted utility is not substantial.

3) to detect metabolic disorders. These asserted utilities are not substantial. The disclosed utility is not substantial because the specification provides no information that the polypeptide SARP3 can accomplish this. The specification teaches how one can use a marker to detect its presence in a sample. However, in the absence of any biological relevance or disease association, mere presence of the SARP3 polypeptide or mRNA encoding a SARP3 polypeptide does not provide a specific and substantial utility for detecting a metabolic disorder. Significant further research would be required of the skilled artisan to perform experiments to establish, if the protein or encoding nucleic acid could be used for detecting a metabolic disorder. Since the asserted utility is not presented in a ready to use, real-world application, the asserted utility is not substantial.

4) to treat subjects suffering from metabolic disorders. Since the polypeptide SARP3 does not have any disclosed biological function and it is expressed in adipose tissue in a mouse model (Example 2, page 68), this does not establish its biological role for any therapeutic intervention. The disclosed polypeptide is an orphan protein for which a real world biological function has yet to be identified. Therefore, treatment of a metabolic disorder using a SARP3 modulator does not have a substantial support. Also, Chang et al. (IDS, Human Mol. Gen 8: 575-583, 1999) disclose that SFRP5, also know as SARP3, is expressed in retinal pigment epithelium (RPE) and may have some role in

wnt signaling. Therefore, any biological relevance of the polypeptide is far from a well established use.

Therefore, the asserted utility of the instantly claimed invention is not established as a substantial and real-world use. Thus, the proposed use of the claimed method is simply a starting point for further research and investigation into potential uses of the polypeptide and any compound that would modulate its activity. See Brenner v. Manon, 148 U.S.P.Q. 689 (Sup. Ct, 1966), wherein the court held that.

Claims 9-11 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Even if the specification disclosed any utility for the claimed polypeptide, it would not enable for a method of modulating a SARP3 mediated lipid metabolism.

The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276

(CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Additionally, the courts have determined that "... where a statement is, on its face, contrary to generally accepted scientific principles", a rejection for failure to teach how to make and/or use is proper (In re Marzocchi, 169 USPQ 367 (CCPA 1971). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977) and have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986).

Among the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed. The instant disclosure fails to meet the enablement requirement for the following reasons:

The Nature of the Invention: The claims are drawn to a method of modulating a SARP3 mediated activity comprising contacting a cell or a tissue that expresses SARP3 with a SARP3 modulator that can modulate lipid metabolism.

The state of the prior art and the predictability or lack thereof in the art:

Lipids and fatty acids play major role in energy balance, hormone synthesis and many metabolic activities. Ranneries et al. (Am. J. Physiology 274: E155- E161, 1998) suggest that any imbalance in fatty acid metabolism can lead to many diseases and disorders. They state that obesity develops due to an interaction between genetic

components and certain environmental factors such as a high fat diet (page E155, 1st paragraph of the left column). It is well known in the art that the low density lipid and triglycerides are high risk factors for many cardio-vascular diseases. Further, obesity is a risk factor for diabetes which is a polygenic disease. Chang et al disclose that the SFRP family comprise many proteins such as SFRP 1-5 (Table 1 on page 576) based on their structure homology. There is no suggestion if any of these proteins can modulate lipid metabolism. Rather Chang et al indicate a possible role of the claimed polypeptide in wnt signaling in eye retina. Therefore, the art indicates that SARP3 is not involved in lipid metabolism.

The amount of direction or guidance present and the presence or absence of working examples: Given the teachings of unpredictability found in the art, detailed teachings are required to be present in the disclosure in order to enable the skilled artisan to practice the claimed invention. These teachings are absent. There is no discussion of how SARP3 can play a role in modulating lipid metabolism and thus, the specification fails to support the assertion of the therapeutic activities of the protein. One of skill in the art would have no starting point to determine how to modulate lipid metabolism. While the specification contains a general discussion on how to screen a compound that could bind or interact with a protein having a known biological function, the specification is totally devoid of any working example in which SARP3 is demonstrated to be involved in lipid metabolism so that it can be applied for treating diabetes or metabolic disorders in a diabetic subject for its contemplated use. The prior

art does not suggest or indicate that the instantly claimed polypeptide SARP3/SFRP5 has any role modulating lipid activity in a subject.

The breadth of the claims and the quantity of experimentation needed:

Because the claims encompass a method of modulating a SARP3 mediated activity comprising contacting a cell or a tissue that expresses SARP3 with a SARP3 modulator that can modulate lipid metabolism, in the light of the teachings of the unpredictability found in the art discussed and because of the supra lack of sufficient teachings in applicants disclosure to overcome those teachings, it would require undue experimentation by one of skill in the art to be able to practice the claimed invention.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gyan Chandra whose telephone number is (571) 272-2922. The examiner can normally be reached on 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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8 May 2006
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